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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,457	08/27/2003	Ronald G. Crystal	216474	5783

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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/649,457	CRYSTAL ET AL.	
	Examiner	Art Unit	
	Marcia S. Noble	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-19,21 and 42-58* is/are pending in the application.

4a) Of the above claim(s) *2,3,11,12 and 42-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1, 6-10, 13-19, and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-3, 6-19, 21, and 42-58 are pending. Claims 1 and 21 are currently amended by Applicant's Response, filed 6/21/2007.

Election/Restrictions

2. Claims 2, 3, 11, 12, and 42-57 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject mater, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/15/2007.

Claims 1-3, 6-10, 13-19, and 21 are under consideration.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. The rejection of claim 6, under 35 U.S.C. 112, second paragraph, as being indefinite for its recitation, "the exotoxin", as lacking antecedent basis, is withdrawn.

Applicant amended claim 1 to recite, "an exotoxin", which clarifies the antecedent basis for claim 6. Therefore, the rejection is withdrawn.

Claim Rejections - 35 USC § 112-1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

8. The rejection of claims 1, 6-10, and 13-19, and 21, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn.

Applicant traverses this rejection on the ground that the art teaches several heterologous sorting signals and signaling peptide. Applicant provides several references with examples of such heterologous sorting and signaling peptides (page 7 of remarks, filed 6/21/2007). Therefore, Applicant's arguments are found persuasive and the rejection is withdrawn.

Enablement

9. Claims 1, 6-10, and 13-19, and 21 as amended, previously presented, and originally presented are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for:

An adenoviral gene transfer vector of serotype 5 comprising a nucleic acid sequence of SEQ ID NO:1 encoding a secretable *B. anthracis* protective antigen comprising human-preferred codons (hPA) and further comprising a nucleic acid sequence encoding a cleavable lysosomal-associated membrane protein –1 sorting

signal (LAMP-1) that targets a protein encoded by the said nucleic acid to the lysosomal pathway, operably linked to the CMV EI promoter-enhancer, does not reasonably provide enablement for:

An adenoviral gene transfer vector comprising a nucleic acid of SEQ ID NO:1 and further comprising 1) any heterologous sorting signal or signal peptide that traffics the encoded protein to any cellular pathway, and 2) lacking a promoter sequence, 3) wherein the gene transfer vector transduces antigen presenting cells, and 4) a pharmaceutical composition comprising said gene transfer vector and a pharmaceutically acceptable carrier, as previously set forth on pages 8-14 of the Office Action, mailed 2/27/2007.

Applicant traverses this rejection on the following grounds:

1) With regards to the heterologous sorting signal and being limited to only LAMP-1, Applicant asserts that the enablement standard does not require that Applicant disclose every operable embodiment of a particular invention, and the application is only required to contain sufficient information regarding the subject matter of the claims so as to enable an artisan to make and use the claimed invention without undue experimentation.

Applicant's arguments have been considered and are not found persuasive. It is acknowledged that Applicant is not required to disclose every operable embodiment. However, the specification does disclose that the instantly claimed vector is meant to elicit an immune response, and therefore the invention requires a heterologous sorting

signal the directs the translated proteins to a cellular compartment involved in antigen presentation. However, the breadth of the claims are drawn to any heterologous sorting signal that directs the translated protein to any compartment, including pathways that would not result in antigen presentation and therefore would not result in the elicitation of an immune response. Therefore, an artisan would not know how to use such a vector to elicit an immune response with such a vector and therefore the specification does not enable such embodiments (see pages 11-12 of Office Action, mailed 2/27/2007).

Applicant also argues that heterologous sorting signals are well established in the art and therefore enabled as a genus. This argument is also not found persuasive, because as previously stated on page 11-12 of the Office Action, mailed 2/27/2007, "the art teaches that the production of fusion proteins to target antigen presenting cells has widely variable means of success depending on the targeting portion of the fusion protein and the species that is immunized. Van Drunen Little-van den Hurk et al (Immunol Rev 199:113-125: 2004) teach that a gene vector encoding a 45W antigen from *Taenia ovis* fused to a CLTA4 targeting polypeptide administered to mice elicited an immune response where as the 45W-L-selectin did not. However, when the 45W-CLTA4 construct was administered to sheep, it did not elicit an immune response (p. 119, col 2 par bridging col 1 and 2). Ultimately, Van Drunen Little-van den Hurk et al (p. 120, col 1, lines 4-6) concluded that "targeting to APC has this far not been effective in natural host species. Therefore, the art suggest that gene transfer vectors that encode fusion protein that have a targeting region that is meant to target it for antigen

presentation and to antigen presenting cell as is the case in the instant invention with the claimed heterologous sorting signals are unpredictable in the art." The specification only provides LAMP-1 as a sorting signal that has been shown to be operable in the instant invention; therefore, the specification only enables LAMP-1 as a sorting signal.

2) Applicant traverses the point of enablement regarding the requirement of a gene therapy vector to have operable linkage to a promoter. Applicant asserts that an artisan of ordinary skill would know that a gene transfer vector would require operable linkage to a promoter; therefore the specification enables the instant invention. Applicant's argument is not found because the claims do not require a promoter and would encompass a gene transfer vector that does not have operable linkage to promoter, which is required for the function of the vector. Because operable linkage to a promoter is required for the function of a gene transfer vector, claims that encompass a gene transfer vector without a promoter would not be enabled because it is well established in the art that they will not function as gene transfer vectors. Therefore, embodiments that lack operable linkage to a promoter are not enabled by the art or specification.

3) Applicant traverses the grounds of enablement encompassing targeting the claimed gene transfer vector to an antigen presenting cell. Applicant points to the specification, which teaches adenoviral vectors with RGD domains or modified RGD domains that can target the adenoviral vector to antigen-presenting cells and thus facilitate infection and transduction of the antigen presenting cells. Applicant's arguments are not found persuasive because the claim does not require the presence

of any adenoviral vector or RGD domains. The breadth of the claims is to a gene transfer vector that does not have any targeting mechanism and still specifically transduces antigen-presenting cells. The art suggests that the functionality of such a vector is relatively small and at best unpredictable. Therefore, the instant invention would not be enabled for a gene transfer vector without any means of targeting to an antigen-presenting cell and that is capable of transducing antigen presenting cells in a targeted fashion (see par bridging page 12 and 13 of the Office Action, mailed 2/27/2007).

4) Applicant traverses that grounds of enablement stating the instant invention is not enabled for a pharmaceutical composition comprising a gene targeting vector. Applicant asserts that the amendment to claim 21 changing "A pharmaceutical composition" to "A composition" obviates this rejection. Applicant's arguments are not found persuasive because claim still recites, "comprising the gene transfer vector of claim 1 and a pharmaceutically acceptable carrier". Because the claims still comprise a pharmaceutically acceptable carrier, the intended use of such a composition is for some treatment. The only treatment disclosed by the specification is to elicit an immune response. The specification does not demonstrate that the claimed vector elicits an immune response in a subject and the art teaches that DNA vaccine is unpredictable (see page 13 and 14 of the Office Action, mailed 2/27/2007). Therefore, the claimed composition is still not enabled.

Therefore, because the amendment to the claims and Applicant's arguments do not overcome the enablement rejection of record, the rejection is maintained.

11. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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